

CLAIMS

2        1. A method for delivering a therapeutic dose of a gene expression  
2 cassette in a fluid selectively to heart for sustained expression comprising  
4 steps of:

4                (a) increasing dwell time of fluid in a targeted area,  
6                (b) administration of a vascular permeablizing agent, and  
8                (c) administration of a viral vector containing a gene expression  
10              cassette of interest.

12        2. A method as in claim 1, wherein the dwell time is increased by the  
14              induction of hypothermia.

16        3. A method as in claim 1, wherein the dwell time is increased by isolation  
18              of the heart from systemic circulation.

20        4. A method as in claim 1, wherein the dwell time is increased by  
22              induction of hypothermia and isolation of the heart from systemic circulation.

24        5. A method as in claim 1, wherein dwell time is increased by induction of  
26              complete or near-complete transient cardiac arrest.

28        6. A method as in claim 1, wherein dwell time is increased by induction of  
30              reversible bradycardia.

32        7. A method as in claim 1, wherein the vascular permeablizing agent is  
34              histamine, substance P or serotonin.

36        8. A method as in claim 1, wherein at least one bolus of virus is  
38              administered.

40        9. A method as in claim 1, wherein the viral vector is an adenoviral vector.

42        10. A method as in claim 9, wherein the adenoviral vector contains a strong  
44              promoter.

2 11. A method as in claim 10, wherein the strong promoter is a  
cytomegalovirus (CMV) promoter.

4 12. A method as in claim 10, wherein the strong promoter is a Rous  
sarcoma virus (RSV) promoter.

6 13. A method as in claim 9, wherein the adenoviral vector contains  
8 enhancer elements.

10 14. A method as in claim 13, wherein the enhancer is a cytomegalovirus  
(CMV) enhancer.

12 15. A method as in claim 13, wherein the enhancer is a Rous sarcoma  
14 virus (RSV) enhancer.

16 16. A method as in claim 1, wherein the viral vector is an adenovirus-  
18 associated viral (AAV) vector.

20 17. A method as in claim 16, wherein the AAV vector contains a strong  
promoter.

22 18. A method as in claim 17, wherein the strong promoter is a  
cytomegalovirus (CMV) promoter.

24 19. A method as in claim 16, wherein the strong promoter is a Rous  
26 sarcoma virus (RSV) promoter.

28 20. A method as in claim 9, wherein the AAV vector contains enhancer  
elements.

30 21. A method as in claim 20, wherein the enhancer is a cytomegalovirus  
32 (CMV) enhancer.

34 22. A method as in claim 20, wherein the enhancer is a Rous sarcoma  
virus (RSV) enhancer.

2            23. A method as in claim 1, wherein the gene of interest is a structural  
gene.

4            24. A method as in claim 23, wherein the structural gene is  $\alpha$ -sarcoglycan.

6            25. A method as in claim 23, wherein the structural gene is  $\beta$ -sarcoglycan.

8            26. A method as in claim 23, wherein the structural gene is  $\gamma$ -sarcoglycan.

10           27. A method as in claim 23, wherein the structural gene is  $\delta$ -sarcoglycan.

12           28. A method as in claim 1, wherein the gene of interest is a functional  
gene.

14           29. A method as in claim 28, wherein the functional gene is  $\beta$ -adrenergic  
receptor ( $\beta$ -AR).

16           30. A method as in claim 28, wherein the functional gene is sarcoplasmic  
reticulum  $\text{Ca}^{2+}$  ATPase (SERCA-2).

20           31. A method as in claim 1, wherein the gene of interest is a gene  
fragment.

22           32. A method as in claim 1, wherein the gene of interest is a mutated form  
of a gene.

24           33. A method as in claim 32, wherein the mutated form of the gene is a  
dominant negative form of phospholamban (PLB).

26           34. A method as in claim 32, wherein the SERCA-2 gene is administered in  
conjunction with a dominant negative form of PLB.

28           35. A method as in claim 33, wherein the dominant negative form of PLB  
contains a mutation at amino acid 2 from glutamic acid (E) to alanine (A).

2        36. A method as in claim 33, wherein the dominant negative form of PLB  
contains a mutation at amino acid 14 from arginine (R) to glutamic acid (E).

4        37. A method as in claim 33, wherein the dominant negative form of PLB  
contains a mutation at amino acid 16 from serine (S) to asparagine (N).

6        38. A method as in claim 33, wherein the dominant negative form of PLB  
contains mutations at amino acid 16 from serine (S) to glutamic acid (E).

10        39. A method as in claim 33, wherein the dominant negative form of PLB  
contains a mutation at amino acid 49 from valine (V) to alanine (A).

12        40. A method as in claim 33, wherein the dominant negative form of PLB  
contains mutations at amino acid 3 from lysine (K) to glutamic acid (E) and at  
amino acid 14 from arginine (R) to glutamic acid (E).

16

18